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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/829,004	04/10/2001	Artur Pedyczak	11014-24/MG	9570

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EXAMINER	
NGUYEN, QUANG	
ART UNIT	**PAPER NUMBER**
1636	13

DATE MAILED: 08/27/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/829,004	PEDYCZAK ET AL.	
	Examiner	Art Unit	
	Quang Nguyen, Ph.D.	1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *19 June 2003* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-22* is/are pending in the application.

4a) Of the above claim(s) *1-4,10,11,14,15 and 17-22* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *5-9, 12-13 and 16* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Claims 1-22 are pending in the present application.

This application contains claims 1-4, 10-11, 14-15, 17-19 and 21-22 drawn to an invention nonelected without traverse in Paper No. 9. A complete reply to the final rejection must include cancelation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01.

Applicants' amendment filed on 6/19/03 has been entered as Paper No. 11.

Amended claims 5-9, 12-13, 16 and 20 are examined on the merits herein, with SEQ ID NO: 9 as the elected species.

The text of those sections of Title 35 U.S.C. Code not included in this action can be found in a prior Office Action.

Response to Amendment

Amended claim 20 is directed to an invention that is independent or distinct from the invention originally claimed for the following reasons: The amended claim 20 is drawn to a method of treating prostate cancer comprising administering to an animal an effective amount of a peptide in accordance with claim 5 (Examiner interprets a peptide in accordance with claim 5 as a recombinant peptide prepared from an isolated nucleic acid molecule of claim 5), classified in class 424, subclass 184.1. This amended claim 20 is distinct from claims originally presented which are directed to a nucleic acid molecule encoding a PSA derived peptide comprising a sequence of the Formula I, an expression vector, an isolated host cell comprising the same as well as methods of

eliciting an immune response and treating cancer using an effective amount of the same nucleic acid molecule, classified in class 514, subclass 44; class 435, subclasses 320.1, 455, for examples.

Since applicant has received an action on the merits for the originally presented invention, this invention has been constructively elected by original presentation for prosecution on the merits. Accordingly, amended claim 20 is withdrawn from consideration as being directed to a non-elected invention. See 37 CFR 1.142(b) and MPEP § 821.03.

Claim Rejections - 35 USC § 102

Amended claims 5-9, 12-13 and 16 remain rejected under 35 U.S.C. 102(b) as being anticipated by Schlom et al. (WO97/35021) for the same reasons already set forth in the previous Office Action.

With respect to the elected species of SEQ ID NO:9, Schlom et al. teach the preparation of a vector comprising at least one insertion site containing a DNA sequence encoding a prostate specific antigen oligo-epitope peptide, operably linked to a promoter capable of expression in a host cell, including prokaryotic and eukaryotic cells (pages 13-14). The DNA sequence encoding a prostate specific antigen oligo-epitope peptide contains or comprises or has SEQ ID NO:9 of the presently claimed invention (see SEQ ID NO:5 on page 64). Schlom et al. also disclose a method for inducing an immune response specific to PSA in the rhesus monkey model using a recombinant vaccinia virus containing the DNA sequence encoding a prostate specific

antigen oligo-epitope peptide to kill prostatic cancer cells (page 17, lines 17-29). Although recombinant pox virus vectors are preferred, other recombinant viral vectors can be utilized including DNA viral vectors such as herpes virus and adenoviruses, and RNA viruses such as retroviruses and polio (page 15, lines 23-24). Schlom et al. also teach that the encoded antigen can be administered into the host with an adjuvant such as cytokines or co-stimulatory molecules or RIBI Deto, QS21 or incomplete Freund's adjuvant or with a suitable carrier such as liposome (page 17, lines 17-30), and that the recombinant vectors will typically injected in a sterile aqueous or non-aqueous solution, suspension or emulsion in association with a pharmaceutically-acceptable carrier such as physiological saline (line 31 on page 19 continues to line 1 of page 20).

Accordingly, Schlom et al. anticipate the instant claimed invention.

Response to Arguments

Applicants' arguments related to the above rejections in the Amendment filed on 6/19/03 in Paper No. 11 (page 5) have been fully considered.

Applicants argue mainly that as defined by Formula I, the encoded PSA derived peptide is at most nine amino acids in length, whereas Schlom's SEQ ID NO:5 encodes a 30 amino acid polypeptide. Therefore, Schlom does not anticipate the instantly claimed invention.

Applicants' argument is respectfully found to be unpersuasive. Please note that the claims are not restricted only to an isolated nucleic acid molecule encoding an immunogenic peptide derived from prostate-specific antigen, wherein the peptide

consists of an amino acid sequence as defined by Formula I, but also to **elongations** of the PSA derived peptide. The term "elongation" refers to any subject peptide having additional amino acid residues added to either end of the peptide (not restricted to any particular number of additional amino acid residues), **preferably** from 1 to 10 amino acid residues, added to either the amino-terminal **and/or** carboxyterminal end of a PSA peptide of the invention (see page 8, lines 7-10).

Accordingly, the instant claims still read on the teachings of Schlom et al. (WO 97/35021), and therefore Schlom et al. still anticipate the instant claims.

Following is a new ground of rejection necessitated by Applicants' amendment.

Claim Rejections - 35 USC § 112

Amended claims 5-9, 12-13 and 16 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an isolated nucleic acid molecule encoding an immunogenic peptide derived from prostate-specific antigen (PSA), the peptide being capable of eliciting an immune response for treating prostate cancer and consisting of an amino acid sequence as defined by Formula I, its elongations, analogs or derivatives of SEQ ID NO:9 (the elected species); and an expression vector, an isolated host cell comprising the same as well as a method of eliciting an immune response in an animal comprising administering an effective amount of the same nucleic acid molecule into an animal, does not reasonably provide

enablement for the same invention with the **encoded peptide fragment less than 8 amino acid residues of SEQ ID NO:9**. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

With respect to the elected invention, the instant claims are drawn to an isolated nucleic acid molecule encoding an immunogenic peptide derived from prostate-specific antigen (PSA), the peptide being capable of eliciting an immune response for treating prostate cancer and consisting of an amino acid sequence as defined by Formula I, its fragments, elongations, analogs or derivatives of the PSA derived peptide, with SEQ ID NO:9 as the elected species; and an expression vector, an isolated host cell comprising the same as well as a method of eliciting an immune response in an animal comprising administering an effective amount of the same nucleic acid molecule into an animal.

The specification teaches by exemplification the nucleic acid sequences of SEQ ID NO:7-12 coding for PSA peptides of SEQ ID NO:1-6, respectively. Applicants further teach that of the six disclosed PSA peptides, 3 peptides having SEQ ID NO:1-3 bind HLA-A0201 molecules on T2 cells, whereas the other 3 peptides containing a binding motif for the gene product HLA-A0201 do not bind to HLA-A0201 molecules on T2 cells. The CLP-312 peptide having SEQ ID NO:3 (encoded by SEQ ID NO:9) is selected as a representative PSA peptide to be injected subcutaneously into A2Kb transgenic mouse to assess the immunogenicity of the HLA-A0201 binding PSA peptide. The results showed that CLP-312 peptide is immunogenic and capable of eliciting an epitope-specific CTL response.

The above evidence has been noted and considered. However, the evidence is not reasonably extrapolated to the instant broadly claimed invention for the reasons discussed below.

(a) The breadth of the claims. The instant claims encompass an isolated nucleic acid molecule encoding an immunogenic peptide derived from prostate-specific antigen (PSA), the peptide being capable of eliciting an immune response for treating prostate cancer and consisting of an amino acid sequence as defined by Formula I, and fragments, elongations, analogs or derivatives of the PSA derived peptide; a vector and isolated host cell comprising the same and a method of eliciting an immune response in an animal using an effective amount of the same nucleic acid molecule.

(b) The state of the prior art and the unpredictability of the art. At the effective filing date of the present application, there is no evidence in the prior art of record that any encoded PSA derived peptide fragment of less than 8 amino acid residues would be capable of eliciting an effective humoral and/or cellular immune response for treating any prostate cancer, including for constituting an effective T-cell epitope that has a sufficient high binding affinity for the class 1 MHC molecules, and for its ability to lodge into the peptide groove of the class 1 MHC molecules to activate efficiently the appropriate subset of CD8+ effector cells for treatment purposes (see WO 97/35021; and Schlom et al., U.S. Patent No. 6,165,460). Please note that as defined by the present application, the term "fragment" refers to any subject peptide having an amino acid residue sequence shorter than that of a PSA peptide of the invention (page 8, lines 3-4). Additionally, Leitner et al. (Vaccine 18:765-777, 2000; Cited previously)

state recently "Although genetic vaccines have been significantly improved, they may not be sufficiently immunogenic for therapeutic vaccination of patients with infectious disease or cancer in clinical trials" (Abstract, page 765).

(c) The amount of direction or guidance presented. Apart from the exemplification showing that the CLP-312 peptide having SEQ ID NO:3 (an epitope having 9 amino acid residues encoded by SEQ ID NO:9) is immunogenic and capable of eliciting an epitope-specific CTL response in A2Kb transgenic mouse, the present disclosure fails to provide sufficient guidance, including any relevant *in vivo* example (part of guidance), showing that an induction of a host immune response against a prostate-specific antigen would be effective for treating a prostate cancer using any PSA prostate epitope having less than 8 amino acid residues, including any PSA epitope encoded by a fragment of the nucleic acid sequence of SEQ ID NO:9. In light of the state of the prior art at the effective filing date of the present application discussed above, and with the lack of sufficient guidance provided by the specification it would have required undue experimentation for a skilled artisan to **use** the instant broadly claimed invention. Furthermore, the physiological art is recognized as unpredictable (MPEP 2164.03). As set forth in *In re Fisher*, 166 USPQ 18 (CCPA 1970), compliance with 35 USC 112, first paragraph requires:

> That scope of claims must bear a reasonable correlation to scope of enablement provided by specification to persons of ordinary skill in the are; in cases involving predictable factors, such as mechanical or electrical elements, a single embodiment provides broad enablement in the sense that, once imagined, other embodiments can be made without difficulty and their performance characteristics predicted by resort to known scientific laws; in cases involving unpredictable factors, such as most chemical reactions and physiological activity, scope of enablement varies inversely with degree of unpredictability of factors involved.

Additionally, the courts have also stated that a reasonable correlation must exist between scope of exclusive right to patent application and scope of enablement set forth in the patent application (27 USPQ2d 1662 *Ex parte Maizel.*).

Accordingly, due to the lack of sufficient guidance provided by the specification regarding to the issues set forth above, the unpredictability of the gene therapy art (specifically genetic vaccine) and the physiological art in general, and the breadth of the claims, it would have required undue experimentation for one skilled in the art to **use** the instant broadly claimed invention.

Claim Rejections - 35 USC § 102

Amended claims 5-9, 12-13 and 16 are rejected under 35 U.S.C. 102(e) as being anticipated by Schlom et al. (U.S. Patent 6,165,460) as evidenced by Schlom et al. (WO97/35021).

With respect to the elected species of SEQ ID NO:9, Schlom et al. (U.S. Patent 6,165,460) disclose the preparation of a recombinant viral vector, preferably a pox virus vector, having at least one insertion site containing a DNA segment encoding prostate specific antigen (PSA) or **a cytotoxic T-cell eliciting epitope thereof**, operably linked to a promoter capable of expression in the host, to generate a specific humoral and cellular immune response to PSA (see Summary of the invention and the claims, particularly claim 5). Although recombinant pox virus vectors are preferred, other recombinant viral vectors can be utilized including DNA viral vectors such as herpes virus and adenoviruses, and RNA viruses such as retroviruses and polio (col. 4, lines

43-45). Schlom et al. teach that the recombinant vectors will typically be injected in a sterile aqueous or non-aqueous solution, suspension or emulsion in association with a pharmaceutically acceptable carrier such as physiological saline (col. 7, lines 20-24). Schlom et al. also teach that the encoded antigen can be administered into the host with an adjuvant such as cytokines or co-stimulatory molecules or RIBI Deto, QS21 or incomplete Freund's adjuvant or with a suitable carrier such as liposome (line 54 of col. 5 continues to line 7 of col. 6). A prostate specific antigen (PSA) specific T cell epitope (PSA 146-154) that has been determined and disclosed by Schlom et al. is the sequence **K-L-Q-C-V-D-L-H-V** (see example II, particularly Tables 6 and 7). A DNA sequence encoding for the aforementioned PSA specific T cell epitope has the same SEQ ID NO:9 of the presently claimed invention as evidenced by the DNA sequence encoding the same T-cell epitope (nucleotides 16-42 of SEQ ID NO:5) taught by Schom et al. (WO97/35021, see SEQ ID NO:5 on page 64).

Accordingly, the instant claims are anticipated by Schlom et al. (U.S. Patent 6,165,460) as evidenced by Schlom et al. (WO97/35021).

Response to Arguments

Applicants' arguments related to the above rejections in the Amendment filed on 6/19/03 in Paper No. 11 (pages 5-6) have been fully considered.

Applicants argue mainly the WO 97/35021 does not anticipate the instantly claimed invention, and therefore the reference can not be properly used as evidence to

support U.S. Patent No. 6,165,460. Applicants' argument is respectfully found to be unpersuasive.

Firstly, please note that the rejection is based on the U.S. Patent No. 6,165,460 issued to Schlom et al., and not on the WO 97/35021 reference. Schlom et al. (U.S. Patent No. 6,165,460) clearly teaches the preparation and use of a recombinant vector having at least one insertion site containing a DNA segment encoding prostate specific antigen (PSA) or **a cytotoxic T-cell eliciting epitope thereof**. A prostate specific antigen (PSA) specific T cell epitope (PSA 146-154) that has been determined and disclosed by Schlom et al. is the sequence **K-L-Q-C-V-D-L-H-V** (see example II, particularly Tables 6 and 7). A DNA sequence encoding for the aforementioned PSA specific T cell epitope has the same SEQ ID NO:9 of the presently claimed invention as evidenced by the DNA sequence encoding the same T-cell epitope (nucleotides 16-42 of SEQ ID NO:5) taught by Schom et al. (WO97/35021, see SEQ ID NO:5 on page 64).

Secondly, the instant claims are not restricted only to an isolated nucleic acid molecule encoding an immunogenic peptide derived from prostate-specific antigen, wherein the peptide consists of an amino acid sequence as defined by Formula I, but also to **elongations** of the PSA derived peptide. The term "elongation" refers to any subject peptide having additional amino acid residues added to either end of the peptide (not restricted to any particular number of additional amino acid residues), **preferably** from 1 to 10 amino acid residues, added to either the amino-terminal **and/or** carboxyterminal end of a PSA peptide of the invention (see page 8, lines 7-10).

Accordingly, the instant claims are anticipated by Schlom et al. (U.S. Patent 6,165,460) as evidenced by Schlom et al. (WO97/35021) for the reasons discussed above.

Conclusion

No claims are allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Quang Nguyen, Ph.D., whose telephone number is (703) 308-8339.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's mentor, David Guzo, Ph.D., may be reached at (703) 308-1906, or SPE, Irem Yucel, Ph.D., at (703) 305-1998.

Quang Nguyen, Ph.D.

DAVID GUZO
PRIMARY EXAMINER